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ITMO Cancer

Key Facts

- ***Team :***

  Researchers : 3
  Technicians : 2
  PhD students : 2
  Postdoc fellows : 0

- ***Translational approaches :***

  Patents : 0
  Clinical research grants : 7
  Industry partners : 0

- ***International research links :***

Keywords

- senescence
- oxidative stress
- autophagy
- ER stress
- tumor stroma
- primary cells
- keratinocytes
- fibroblasts
- DNA damage
- tumorigenesis assays

Biological resources

Corinne Abbadie

Initiation of Epithelial Cancers

/ / de Launoit Yvan

CNRS / University / Pasteur Institute of Lille

We are working on the molecular mechanisms of tumorigenesis by senescence evasion with in vitro culture models of normal human cells

Research brief

Initially described as the phase reached by cultivated human normal fibroblasts after a finite number of passages, cellular senescence is now recognized as a fundamental program that can be activated in many cell types in response to telomere dysfunction, DNA damage, oxidative stress, or activation of oncogenes, such as Ras or NF-kappaB.

Senescence is assumed to be an irreversible growth arrest state that cells have to bypass to generate tumors. However, senescence is not irreversible in all cell types, notably in epithelial cells that are at the origin of the most frequent cancers in humans. Indeed, we and others have shown that although they display all the characteristics of senescent cells, normal human epidermal keratinocytes or mammary epithelial cells that have reached the senescence plateau can spontaneously reactivate a mitotic process to generate so-called post-senescence (PS) emerging cells, which are transformed and able to form skin hyperplasias and carcinomas in nude mice. Data from our group suggest that the oxidative DNA damage encountered by senescent cells could be the mutagenic motor underlying this neoplastic escape. We are presently working at characterizing these oxidative DNA damages. Besides, we and others have shown that senescence in fibroblast is associated with a complete change in the secretome. Our current analyses show that this secretome enhances the epithelial-to-mesenchymal transition of the PS-emergent cells.

Methodologies used

- in vitro culture of normal human cells
- molecular biology (PCR, western-blotting...)
- cellular imaging
- cytometry
- comet assays
- migration and invasion assays
- in vivo tumorigenesis assays
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Publications

- S. Zdanov, D. Bernard, F. Debacq-Chainiaux, S. Martien, K. Gosselin, C. Vercamer, F. Chelli, O. Toussaint and C. Abbadie (2007). Normal or stress-induced fibroblast senescence involves COX-2 activity. Exp Cell Res, 313, 3046-56
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- N. Humbert, S. Martien, A. Augert, M. Da Costa, S. Mauen, C. Abbadie, Y. de Launoit, J. Jil and D. Bernard (2009). A genetic screen identifies Topoisomerase 1 as a regulator of senescence. Cancer Research, 69, 4101-6.
- K. Gosselin, S. Martien, A. Pourtier, C. Vercamer, P. Ostoich, L. Morat, L. Sabatier, L. Duprez, C. T?Kint de Roodenbeke, E. Gilson, N. Malaquin, N. Wernert, P. Slijepcevic, M. Ashtari, F. Chelli, E. Deruy, B. Vandenbunder, Y. de Launoit and C. Abbadie (2009). Senescence-associated oxidative DNA damage promotes the generation of neoplastic cells. Cancer Research, 69, 7917-7925
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- E. Deruy, K. Gosselin, C. Vercamer, S. Martien, F. Bouali, C. Slomianny, J. Bertout, D. Bernard, A. Pourtier and C. Abbadie (2010). MnSOD upregulation induces autophagic programmed cell death in senescent keratinocytes. PlosOne, 5, e12712.

Patents, pending/registered

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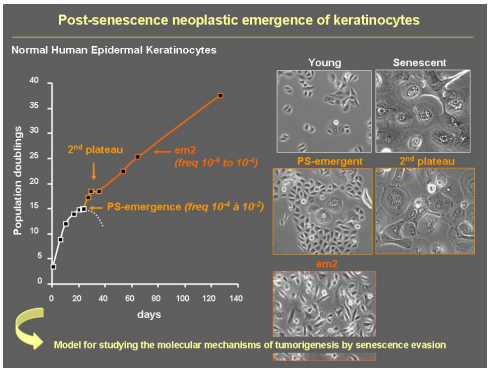
In vitro model for studying the molecular mechanisms of tumorigenesis by senescence evasion



Impact of the aging tumor stroma on the post-senescence neoplastic emergence of keratinocytes